

## **REMARKS**

### **Claim Rejections – 35 U.S.C. § 112, First Paragraph (Enablement)**

The Examiner rejected claims 1-54, 61 and 62 under 35 U.S.C. § 112, First Paragraph, as failing to comply with the enablement requirement because the claims contain subject matter was not described in the specification in such a way as to enable one skill in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the Examiner contended that the instant claims are not enabled because the specification fails to teach how to identify an unknown candidate antagonist as true antagonist and its chemoattractant receptor following the BiRAM and MultiRAM assays, and as such a large quantity of experimentation would be necessary to identify a candidate antagonist as a true antagonist and its chemoattractant receptor.

Applicants disagree with the Examiner's conclusion that practicing the invention would necessarily entail undue experimentation. The enablement rejection raised of "undue" experimentation clearly presents support in itself that experimentation is acceptable in practicing a valid claim – just how much remains at issue. Indeed, it is known that even a "considerable amount of experimentation is permissible." *In re Wands*, 858 F.2d 731,737 (Fed.Cir. 1988). The issue on experimentation can resolve to determine whether the experimentation is "merely routine" or, in the event of non-routine experimentation required, does "the specification provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." *Ibid*.

Here, the practice of Applicants' invention may require, at most, routine experimentation because the specification fully enables the scope of the claims 1-27 and 61 that are directed to methods for identifying chemoattractant receptor antagonists, the methods including the steps of providing an apparatus comprising an upper chamber and a lower chamber separated by a porous membrane, placing a candidate antagonist and either a single cell population comprising first and second chemoattractant receptors (as in claims 1-26 and 61) or two different cell populations each comprising a different chemoattractant receptor (as in claim 27) in the upper

chamber, placing an inhibitory concentration of a ligand for the first chemoattractant receptor in the lower chamber, placing an inhibitory concentration of a ligand for the second chemoattractant receptor in the lower chamber, monitoring movement of the cell population from the upper chamber to the lower chamber, wherein the movement identifies the candidate antagonist as an antagonist of at least one of the first and second chemoattractant receptors, and determining whether an identified antagonist is an antagonist for one of the first chemoattractant receptors, the second chemoattractant receptor, or both (as in claims 1-26).

Similarly, only a routine experimentation may be needed to practice Applicants' invention of claims 28-54 and 62 because the specification fully enables the scope of claims directed to methods for identifying chemoattractant receptor, the methods including the steps of providing an apparatus comprising an upper chamber and a lower chamber separated by a porous membrane, placing a candidate antagonist and a first cell population and a second cell population in the upper chamber, wherein the first cell population comprises a first chemoattractant receptor and wherein the second cell population comprises a second chemoattractant receptor; placing an inhibitory concentration of a ligand for the first chemoattractant receptor in the lower chamber; placing an inhibitory concentration of a ligand for the second chemoattractant receptor in the lower chamber; monitoring movement of the first and the second cell populations from the upper chamber to the lower chamber, wherein the movement identifies the candidate antagonist as an antagonist of at least one of the first and second chemoattractant receptors; and determining whether an identified antagonist is an antagonist for one of the first chemoattractant receptors, the second chemoattractant receptor, or both.

First, Applicants have provided reasonable guidance to help one skilled in the art to conduct that experimentation so that any necessary experimentation is simply routine experimentation. Specifically, throughout the specification, Applicants provide ample description of BiRAM and MutiRAM assays that may be used to identify candidate antagonist hits to chemoattractant receptors. See instant specification at pages 18 through 21, first paragraph for BiRAM assay; and pages 21, second paragraph, through page 22, lines 1-4 for MultiRAM assay. Moreover, Applicants

further provide, for instance, at pages 39-43 specific examples (Examples 8, 9 and 10) of BiRAM screening assays.

Although, the identity of the chemoattractant receptor(s) reacting in the assay and causing cell migration is not known immediately following the BiRAM and MultiRAM assays, Applicants teach, for example, at page 20, 1<sup>st</sup> full paragraph, and page 22, lines 1-4 of the instant specification, that RAM assay (i.e., UniRAM) may be employed for re-screening of the candidate antagonists. In the RAM assay only one ligand is applied at a time. The RAM assay is described in detail at page 16, last paragraph, through page 18, lines 1-2. See also Figures 8 and 9 illustrating the use of RAM assay for identification of unknown antagonists as true antagonists to chemoattractant receptors.

Moreover, at page 25, lines 1-14, Applications disclose additional assay methods, such as conventional HTS methods, such as FLIPR™ that measure calcium mobilization, or a cell migration assay (chemotaxis assay), and may be used for discriminating true chemoattractant receptor antagonist hits.

Accordingly, one of skill in the art, following the BiRAM and MultiRAM assays, would be able to identify unknown candidate antagonists as true antagonists and their chemoattractant receptors using RAM assay described in detail in the instant specification, as well as, in the U.S. Pat. Application Serial No. 10/154,399, filed on May 22, 2002 (published under U.S. Pat. Pub. No. 2003-017485-A1), which was incorporated by reference in its entirety into the instant specification, or a conventional assay, such as FLIPR™ (Spec. page 25, line 7).

Particularly in view of the aforementioned recital of guidance found in the specification of specific assay methods that can be used to identify unknown candidate antagonists as true antagonists and their chemoattractant receptors, and the fact of actual examples, Applicants respectfully submit that the enablement rejection of claims 1-54, 61, and 62 should be withdrawn.

#### **Claim Rejections – 35 U.S.C. § 112, Second Paragraph (Indefiniteness)**

The Examiner rejected claim 1 under 35 U.S.C. § 112, Second Paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter

which applicant regards as the invention. Specifically, the Examiner asserted that the instant claims are indefinite because of the interchangeable use of "placing a candidate antagonist and a cell population" (as in claims 1, 2, 3, 19-21, 28, 29, 46-48, and 54) and "incubating a candidate antagonist and a cell population" (as in claim 27) and because it is unclear from the specification, the difference between "placing" and "incubating."

Applicants disagree with the Examiner. Nonetheless, Applicants amended claim 27 to replace word "incubating" with word "placing." In view of the aforementioned amendment to claim 27, Applicants request that the 112, Second Paragraph indefiniteness rejection of claim 1, be withdrawn.

### **Claim Objections**

The Examiner objected to claims 27, 28, and 54. Specifically, the Examiner asserted that these claims include very similar steps and raise the question of similar scope.

Applicants disagree with the Examiner. Nonetheless, Applicants amended claims 27 and 54 to clarify that the determining step may be performed by a RAM assay. RAM assay is described in detail throughout the specification including for example at page 16, lines 20-31 and continuing through page 18, lines 1-2.

Because claims 27 and 54 depend from claims 1 and 28, respectively, which are directed to two distinct BiRAM assay formats (Spec. page 18, lines 6-10), these claims are distinct. Specifically, claim 27 depends from claim 1, which is generally directed to a BiRAM where **a single cell population** expressing two different chemoattractant receptors is used (Spec. page 18, lines 6-10). Claim 27 further defines the 'determining step' of claim 1. Claim 28 differs from claim 27 because it is generally directed to a BiRAM assay that uses **two distinct cell populations**, each expressing a different chemoattractant receptor (Spec. page 18, lines 6-10). Claim 54 further defines the 'determining step' of claim 28.


In view of the amendment to claims 27 and 54 and remarks provided above, Applicants request that the claim objections be withdrawn.

**CONCLUSION**

Applicants respectfully submit that present application is now in condition for allowance. Should the Examiner feel a discussion would expedite the prosecution of this application, the Examiner is kindly invited to contact the undersigned at (312) 245-5398.

Respectfully submitted,

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